REMARKS

Claims 1-4 and 18-33 are pending in the application. The amendments to the claims have been made to further clarify the present invention and conform the application to U.S. practice. Support for the newly added claims 20-23 can be found in claim 17 as originally presented. Support for newly added claims 24-27 can be found at *inter alia*, page 17 in the present specification. Support for the newly added claims 28-31 can be found at *inter alia*, pages 18-20 in the present specification. Support for newly added claim 32 can be found at *inter alia*, page 15 in the present specification. Support for the newly added claim 33 can be found at *inter alia*, page 14 in the present specification. No new matter has been inserted into the application.

Restriction Requirement

Applicants acknowledge Examiner's decision to rejoin the claims of Groups I-III (claims 1-3 and 17) with the claims of Group IV (claims 4 and 17).

Information Disclosure Statement

In compliance with 37 CFR 1.98(a)(1), Applicants have enclosed various references and form PTO-1449 for the Examiner's consideration and signature.

Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1-4 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicants traverse this rejection. However, claims 1-4 have been currently amended to point out and distinctly claim the subject matter which applicant regards as the invention. Therefore, this rejection has been overcome.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-4 and 17 have been rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not provide enablement for LK6, LK7 or LK8 protein comprising various domains and functionally equivalent domains. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Claims 1-4 and 17 have been further rejected under 35 U.S.C. §112, first paragraph for allegedly containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

In the present application, Applicants have discovered that isolated kringle domains LK6, LK7, LK8 and their combination LK68 provide an unexpected result of inhibiting capillary development, inhibiting endothelial cell proliferation and migration, and suppressing tumor growth, which are all related to the inhibition of angiogenesis. The claims in the present application are directed to a polypeptide consisting of human apolipoprotein(a) kringle domains IV36, IV37, V38 or a combination of these domains. Thus, Applicants submit that the specification fully enables the invention and shows possession of these polypeptides.

Rejection Under 35 U.S.C. §102(b) over Cao

Claim 17 has been rejected under 35 U.S.C. §102(b) as being anticipated by Cao et al (*J* Biol. Chem. 272:22924-22928, 1997). Applicants traverse this rejection. However, claim 17 has been canceled. Therefore, this rejection has been overcome.

Rejection Under 35 U.S.C. §102(b) over Mikol

Claims 2 and 17 have been rejected under 35 U.S.C. §102(b) as being anticipated by Mikol (J Mol Biol. 256(4):751-61, 1996). Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Mikol discloses crystallizing human apolipoprotein(a) kringle type IV37 ($K4_{37}$) in order to obtain its crystal structure. Mikol discloses concentrating Apo(a)$K4_{37}$ in 80 mM NaCl, 0.02% (w/v) NaN_3.

The Examiner is reminded that in order to reject a claim under §102, each and every element in the claim must be disclosed in the cited reference. In the instant application, Applicants note that the amino acid sequence of apolipoprotein(a) $K4_{37}$ that is disclosed in the Mikol reference and the LK7 polypepide that is claimed in the present application are different. For instance, the N-terminus of Mikol's apolipoprotein(a) $K4_{37}$ has additional amino acid residues, GSHM, compared with Applicants' LK7. Also, the C-terminus of Mikol's apolipoprotein(a) $K4_{37}$ lacks amino acid residue V, compared with that of LK7. Moreover, Mikol fails to disclose or suggest any anti-angiogenic activity associated with apolipoprotein(a) or the apolipoprotein(a) LK7 domain as in the present invention. Thus, Mikol fails to anticipate the claimed invention.

In addition to the above, in the Office action of April 9, 2003, the Examiner also rejected claim 17 for reciting "pharmaceutically acceptable carrier", and indicated that Mikol discloses a pharmaceutically acceptable carrier. Insofar as this type of rejection may be reapplied against newly added claims 20-23, which recite such "pharmaceuticaly acceptable carrier" language, Applicants note that the rationale for the Examiner's rejection of "pharmaceutically acceptable carrier" is based on a misreading of Mikol. The Examiner has pointed to page 759 in Mikol as

disclosing a pharmaceutically acceptable carrier for the Apo(a)$K4_{37}$ polypeptide because Apo(a)$K4_{37}$ polypeptide is found in 80 mM NaCl solution, which the Examiner considers to be a pharmaceutically acceptable carrier. However, a careful reading of Mikol at the indicated location at page 759, right column indicates that Apo(a)$K4_{37}$ is not placed in 80 mM NaCl at all, but rather in a solution that includes 80 mM NaCl together with the well-known poison NaN_3 (0.02% (w/v)). NaN_3 is recognized as a known poison even in minute quantities. (See attached Exhibit A). A person of skill in the art would not consider the 80 mM NaCl, 0.02% (w/v) NaN_3 solution disclosed in Mikol to be fit to be used as a pharmaceutically acceptable carrier. Thus, Mikol fails to disclose or suggest a pharmaceutically acceptable carrier.

Rejection Under 35 U.S.C. §102(b) over Kraft

Claim 2 has also been rejected under 35 U.S.C. §102(b) as being anticipated by Kraft (Human Genetics. 95:275-282, 1995). Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Kraft discloses polymorphism associated with alleles of human apolipoprotein(a) kringle IV37 using the technique of pulsed field gel electrophoresis. However, Kraft fails to disclose or suggest producing the kringle IV37 polypeptide itself. Kraft further fails to disclose or suggest any anti-angiogenic activity associated with any LK7 polypeptide that may be produced. Thus, Kraft fails to anticipate the presently claimed invention.

Rejection Under 35 U.S.C. §102(b) over McLean

Claims 1-4 have been rejected under 35 U.S.C. §102(b) as being anticipated by McLean (Nature 33:132-137, 1987). Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested.

McLean discloses cDNA sequence of human apolipoprotein(a). However, McLean fails to disclose or suggest producing the kringle polypeptide itself. McLean further fails to disclose or suggest that any such produced polypeptide may have any anti-angiogenic activity. Thus, McLean fails to anticipate the presently claimed invention.

Rejection Under 35 U.S.C. §103(a) over McLean in view of USP '963 (U.S. Patent No. 6,413,963)

Claim 17 has been rejected as being obvious over McLean (Nature 33:132-137, 1987) in view of USP '963. Applicants traverse this rejection. Reconsideration and withdrawal thereof are respectfully requested. Applicants note that claim 17 has been canceled. Therefore, this rejection has been overcome. However, insofar as the instant rejection may be applicable to the newly presented claims 20-23, Applicants provide the following comments.

McLean is described above.

USP '963 is cited for the disclosure of a pharmaceutically acceptable carrier.

Applicants submit that the Examiner has failed to establish *prima facie* obviousness over the cited references. In view of the fact that McLean fails to disclose or suggest the production of LK6, LK7, LK8 and LK68 as in the presently claimed invention, and that USP '963 fails to remedy this deficiency, USP '963 fails to be combinable with McLean. Accordingly, the present invention is not obvious over McLean in combination with USP '963.

Conclusion

It is believed that the application is now in condition for allowance. Applicants request the Examiner to issue a notice of Allowance in due course. The Examiner is encouraged to contact the undersigned to further the prosecution of the present invention.

The Commissioner is authorized to charge JHK Law's Deposit Account No. 502486 for any fees required under 37 CFR §§1.16 and 1.17 that are not covered, in whole or in part, by a credit card payment enclosed herewith and to credit any overpayment to said Deposit Account No. 502486.

Date: August 11, 2003 (Monday)

Respectfully submitted,

JHK Law
P.O. Box 1078
La Canada, CA 91012-1078
Telephone: 818-952-7430
Facsimile: 818-952-7424

Joseph Hyosuk Kim, Ph. D.
Registration No. 41,425

Enclosure: Exhibit A